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2352 7590 03/19/2009

OSTROLENK FABER GERB & SOFFEN
1180 AVENUE OF THE AMERICAS
NEW YORK, NY 100368403

EXAMINER

GEBREYESUS, KAGNEW H

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 03/19/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/532,948

01/09/2006

Shigeyuki Yokoyama

P/2850-106

2037

TITLE OF INVENTION: METHOD OF EXPRESSING PROTEIN HAVING UNNATURAL AMINO ACID INTEGRATED THEREINTO

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	06/19/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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2352 7590 03/19/2009

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1180 AVENUE OF THE AMERICAS
NEW YORK, NY 100368403

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/532,948 01/09/2006 Shigeyuki Yokoyama P/2850-106 2037

TITLE OF INVENTION: METHOD OF EXPRESSING PROTEIN HAVING UNNATURAL AMINO ACID INTEGRATED THEREINTO

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
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nonprovisional NO \$1510 \$300 \$0 \$1810 06/19/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
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GEBREYESUS, KAGNEW H 1656 435-183000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____
- 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____

Date _____

Typed or printed name _____

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This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,948	01/09/2006	Shigeyuki Yokoyama	P/2850-106	2037
2352	7590	03/19/2009	EXAMINER	
OSTROLENK FABER GERB & SOFFEN 1180 AVENUE OF THE AMERICAS NEW YORK, NY 100368403			GEBREYESUS, KAGNEW H	
			ART UNIT	PAPER NUMBER
			1656	
DATE MAILED: 03/19/2009				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability

Application No.

10/532,948

Applicant(s)

YOKOYAMA ET AL.

Examiner

KAGNEW H. GEBREYESUS

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 2/6/09.
2. ☒ The allowed claim(s) is/are 1, 6, 7, 8, 13.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>2/6/09</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 06, 2009 has been entered. Claim 1 has been amended. Claims 1 and 6-16 are pending in the present application.

All objections and rejections from the prior Office Action have been withdrawn. Restriction between group I and group II has been withdrawn and the claims rejoined.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Mark A. Farley on March 10, 2009.

Claim 1 (currently amended): An expression method for non-naturally-occurring amino acid-containing proteins comprising: expressing in isolated animal cells:

(A) a mutant tyrosyl-tRNA synthetase (~~V37-C195~~) ~~that has undergone alterations comprising a~~ substitution from tyrosine to valine at position 37 and ~~from~~ glutamine to cysteine at position 195

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(V37C195) ~~of~~ in the tyrosyl tRNA synthetase of SEQ ID NO:29 wherein said synthetase has with an enhanced specificity for a non-naturally-occurring tyrosine derivative selected from the group consisting of 3-iodotyrosine and 3-bromotyrosine, as compared ~~with~~ to the specificity for tyrosine;

(B) *Bacillus stearothermophilus* suppressor tyrosyl tRNA (tRNA^{Tyr}) capable of ~~binding~~ being aminoacylated with the tyrosine derivative in the presence of the mutant tyrosyl tRNA synthetase; and,

(C) a gene encoding a desired protein ~~gene that has undergone~~ comprising a nonsense mutation at a desired site; wherein, the tyrosine derivative is incorporated in the desired protein in response to the ~~created~~ nonsense ~~codon~~ mutation.

Claim 6 (previously presented): The expression method according to claim 1 wherein the isolated animal cells are mammalian cells.

Claim 7 (currently amended): A ~~non-naturally-occurring amino acid-containing protein production~~ method of producing in isolated animal cells a protein comprising a tyrosine derivative incorporated at a desired site comprising:

a) expressing the protein according to the method of claim 1; and [[:]]

b) recovering and purifying [[a]] the protein. ~~expressed in an isolated animal cell according to the method according to claim 1.~~

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Claim 8 (currently amended): An isolated ~~Animal~~ animal cell[[s]] containing:

(A) an expression vector that expresses in the animal cell[[s]] a mutant tyrosyl-tRNA synthetase comprising a substitution from tyrosine to valine at position 37 and glutamine to cysteine at position 195 that is a derivative of tyrosyl tRNA synthetase from E. coli with an enhanced specificity for a non-naturally-occurring tyrosine derivative (V37C195) in the tyrosyl tRNA synthetase of SEQ ID NO:29 wherein said synthetase has enhanced specificity for a non-naturally-occurring tyrosine derivative selected from the group consisting of 3-iodotyrosine and 3-bromotyrosine as compared with the specificity for tyrosine;

(B) an expression vector that expresses in the animal cell[[s]] a ~~suppressor tRNA originating in a~~ Bacillus species, Mycoplasma species or Staphylococcus species of eubacteria *Bacillus stearothermophilus* suppressor tyrosyl tRNA (tRNA^{Tyr}) capable of ~~binding~~ being aminoacylated with the tyrosine derivative in the presence of the mutant tyrosyl tRNA synthetase; and,

(C) an expression vector that expresses in the animal cells a desired protein ~~gene that has undergone~~ from a gene comprising a nonsense mutation at a desired site; and wherein, the tyrosine derivative is incorporated in the protein at the site of the nonsense mutation in the gene of the protein .

Claims 9-12 (cancel).

Claim 13 (currently amended): The isolated animal cells according to claim 8 that are mammalian cells.

Claims 14-16 (cancel).

Conclusion

Claims 1, 6, 7, 8, and 13 are allowed.

Reason for allowance

An in-vivo eukaryotic cell based method that specifically uses a tRNA synthetase mutant (V37C195) from *E. coli* in combination with the *B. stearothermophilus* tRNA which possesses both a box A and box B in the promoter region (which promoter is also expressed in the tRNA) to produce a protein in a cell makes this invention distinguishable from the art (Kiga et al. and US 7393670 B2) that teaches an in-vitro translation system that uses the tRNA synthetase mutant (V37C195) and tRNA from *E. coli* that only function in an in-vitro translation system and not in an in-vivo cell based system.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656
2/10/2009

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657